Testimony
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AVIAN INFLUENZA: Preparing for a Possible Influenza Pandemic

Statement of

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Mr. Chairman and members of the Committee, I am pleased to be here today to describe the current status of avian influenza around the world; the consequences of a possible human influenza pandemic; and international and domestic efforts to prepare for, and respond to such a pandemic, including the *HHS Pandemic Influenza Plan*. Thank you for the invitation to testify on influenza pandemic planning and preparedness which Department of Health and Human Services (HHS) Secretary Mike Leavitt has made a top priority. The Centers for Disease Control and Prevention (CDC) and other agencies within HHS are working together formally through the Influenza Preparedness Task Force that Secretary Leavitt has chartered to prepare the United States for this potential threat to the health of our nation. We are also working with other federal, state local and international organizations to ensure close collaboration.

As you are aware, the potential for a human influenza pandemic is a current public health concern with an immense potential impact. Inter-pandemic (seasonal) influenza causes an average of 36,000 deaths each year in the United States, mostly among the elderly, and more than 200,000 hospitalizations. In contrast, scientists cannot predict the severity and impact of an influenza pandemic, whether from the H5N1 virus currently circulating in Asia and Europe, or the emergence of another influenza virus of pandemic potential. However, modeling studies suggest that, in the absence of any control measures, a "medium-level" pandemic in which 15 percent to 35 percent of the U.S. population develops influenza could result in 89,000 to 207,000 deaths, between 314,000 and 734,000 hospitalizations, 18 to 42 million outpatient visits, and another 20 to 47 million sick people. The associated economic impact in our country alone could range between $71.3 and $166.5 billion. A more severe pandemic, as happened in 1918, could have a much greater impact.

There are several important points to note about an influenza pandemic:

- A pandemic could occur anytime during the year and could last much longer than typical seasonal influenza, with repeated waves of infection that could occur over one or two years.
- The capacity to intervene and prevent or control transmission of the virus once it gains the ability to be transmitted from person to person will be extremely limited.
- Right now, the H5N1 avian influenza strain that is circulating in Asia among birds is considered the leading candidate to cause the next pandemic. However, it is possible that another influenza virus, which could originate anywhere in the world, could cause the next pandemic. Although researchers believe some viruses are more likely than others to cause a pandemic, they cannot predict with certainty the risks from specific viruses. This uncertainty is one of the reasons why we need to maintain year-round laboratory surveillance of influenza viruses that affect humans.
- We often look to history in an effort to understand the impact that a new pandemic might have, and how to intervene most effectively. However, there have been many changes since the last pandemic in 1968, including changes in population and social structures, medical and technological advances, and a significant increase in international travel. Some of these changes have increased our ability to plan for and respond to pandemics, but other changes have made us more vulnerable.
- The current threat of a human pandemic due to HPAI H5N1 should be addressed at both the human and animal levels, recognizing that this is currently an animal

disease. But because pandemic influenza viruses will emerge in part or wholly from among animal influenza viruses, such as birds, it is critical for human and animal health authorities to closely coordinate activities such as surveillance and to share relevant information as quickly and as transparently as possible.

The Current Status of H5N1 Virus in Asia

Beginning in late 2003, new outbreaks of lethal highly pathogenic avian influenza A (HPAI H5N1) infection among poultry and waterfowl were reported by several countries in Asia. In 2005, outbreaks of HPAI H5N1 disease have also been reported among poultry in Russia, Kazakhstan, Turkey, and Romania. Mongolia has reported outbreaks of the H5N1 virus in wild, migratory birds. In October 2005, outbreaks of the H5N1 virus were reported among migrating swans in Croatia. In 2004, sporadic human cases of avian influenza A (H5N1) were reported in Vietnam and Thailand. In 2005 additional human cases have been reported in Cambodia, China, Indonesia, Thailand, and Vietnam. Cumulatively, as of December 6, 2005, 134 human cases have been reported and laboratory confirmed by the World Health Organization (WHO) since January 2004. These cases have resulted in 69 deaths, a fatality rate of approximately 51 percent. Almost all cases of H5N1 human infection appear to have resulted from some form of direct or close contact with infected poultry, primarily chickens. In addition, a few persons may have been infected through very close contact with another infected person, but this type of transmission has not led to sustained transmission.

For an influenza virus to cause a pandemic, it must: (1) be a virus to which there is little or no pre-existing immunity in the human population; (2) be able to cause illness in humans; and, (3) have the ability for *sustained* transmission from person to person. So far, the HPAI H5N1 virus circulating in Asia meets the first two criteria but has not yet shown the capability for sustained transmission from person to person.

The highly pathogenic avian influenza A (H5N1) epizootic (or animal) outbreak in Asia that is now beginning to spread into Europe is not expected to diminish significantly in the short term. It is likely that H5N1 infection among birds has become endemic in certain countries in Asia and that human infections resulting from direct contact with infected poultry will continue to occur. So far, scientists have found no evidence for genetic reassortment. Reassortment can occur when the genetic code for high virulence in an H5N1 strain combines with the genetic code of another influenza virus strain resulting in a new virus that is more easily transmitted. However, the animal outbreak continues to pose an important public health threat, because there is little preexisting natural immunity to H5N1 infection in the human population.

In October 2005, CDC Director Julie Gerberding accompanied HHS Secretary Mike Leavitt when he led a delegation of U.S. and international health experts on a 10-day trip to five nations in Southeast Asia. The purpose of this trip was: 1) to learn from countries that have had first-hand experience with avian influenza; 2) to emphasize the importance of timely sharing of information in fighting the disease; and, 3) to determine the best use of

our resources abroad to protect people in the United States. They learned several important lessons. First, international cooperation is absolutely essential; an outbreak anywhere increases risk everywhere. Second, surveillance, transparency, and timely sharing of information are critical. The ability of the United States and the world to slow or stop the spread of an influenza pandemic is highly dependent upon early warning of outbreaks. Finally, it is vital to strengthen preparedness and response capabilities in Asian countries and other parts of the world. The delegation also concluded that pandemic preparedness and preparation must be both short- and long-term in scope. These critical elements form the basis of the Administration's diplomatic engagement strategy through the International Partnership on Avian and Pandemic Influenza, launched by the President in September, and drive our efforts with the international health community to prepare effectively for a pandemic. As I stated earlier, there is no way to know if the current H5N1 virus will evolve into a pandemic. However, we do know that there have been three pandemics in the past 100 years, and we can expect more in this century.

HHS Role in International Preparedness

The Secretary's trip reaffirmed the value of several actions undertaken by HHS and its agencies over the last few years. It is vital to monitor H5N1 viruses for changes that indicate an elevated threat for humans, and we are continuing to strengthen and build effective in-country surveillance, which includes enhancing the training of laboratorians, epidemiologists, veterinarians, and other professionals, as well as promoting the comprehensive reporting that is essential for monitoring H5N1 and other strains of highly pathogenic avian influenza. In collaboration with international partners and other U.S. Government Agencies, HHS is also pursuing a strategy of active, aggressive international detection; investigation capacity; international containment; and laboratory detection support.

In the past year, working with the World Health Organization (WHO), other U.S. Government and international partners, HHS and its agencies have made significant progress toward enhancing surveillance in Southeast Asia. However, this initiative needs to continue at both national and international levels if we are to sustain our progress, expand geographic coverage, and conduct effective surveillance. These efforts to build international and domestic surveillance are essential for detecting new influenza virus variants earlier and for making informed vaccine decisions about inter-pandemic influenza. With the ever-present threat of a newly emerging strain that could spark a human pandemic, we need to know what is happening in commercial poultry farms and the family backyard flocks found in Southeast Asia, as well as migrating birds and animal populations elsewhere throughout the world.

Earlier this year, Congress passed and the President signed the Fiscal Year 2005 Emergency Supplemental Appropriations Act for Defense, the Global War on Terror, and Tsunami Relief. This legislation includes $25 million in international assistance funds for HHS, the U.S. Department of Agriculture (USDA), and the United States Agency for

International Development (USAID) to prevent and control the spread of avian influenza in Asia. With these funds, HHS and its agencies are working to assist in developing regional capacity in Southeast Asia for epidemiology and laboratory management of pandemic influenza. Strategies include developing and implementing an avian influenza curriculum for epidemiologists and laboratorians, training for public health leaders to develop a national network of public health field staff, and training for local allied health personnel to detect and report human cases of influenza. HHS staff are being assigned to Vietnam, Cambodia, and Laos to facilitate improvements in the detection of influenza cases and to provide technical assistance in investigating cases and in developing national preparedness plans by the Ministries of Health, with the assistance of WHO and other partners.

We are also working with USAID, WHO Secretariat, WHO's Regional Offices and Ministries of Health in these countries to increase public awareness about the human health risks associated with pandemic influenza, and to advise countries concerning prevention or mitigation measures that can be used in the event a pandemic occurs.

HHS, through CDC, is vigorously working to increase laboratory capacity in the region and to provide laboratory support for outbreak investigations, including: a) testing clinical samples and influenza isolates, b) diagnosing the presence of avian influenza in humans by supplying necessary test reagents to the region and globally, and c) developing vaccine seed stock to produce and test pandemic vaccine candidates. HHS's National Institutes of Health (NIH) and Office of Public Health Emergency Preparedness are also providing technical assistance to the government of Vietnam as it proceeds with the development of a human H5N1 vaccine, including support for clinical trials

CDC is one of four WHO Global Influenza Collaborating Centers. In this capacity, CDC conducts routine worldwide monitoring of influenza viruses and provides ongoing support for the global WHO surveillance network, laboratory testing, training, and other actions. HHS and USAID also support the WHO Headquarters in Geneva and the WHO Regional Offices in Manila and New Delhi for pandemic planning, expansion of global influenza surveillance, shipment of specimens, training, and enhancing communications with agricultural authorities. Several of the top flu specialists on the WHO staff are HHS personnel on loan, another demonstration of our strong commitment to international collaboration in the fight against the threat of a pandemic influenza.

In addition to our partnership with USAID under the Tsunami supplemental appropriation, HHS also partners with other U.S. Government departments in its international collaboration, such as with the Department of Defense Naval Medical Research Unit Two (NAMRU2) in Indonesia and Naval Medical Research Unit Three in Cairo (NAMRU3). These collaborations support training, the expansion of influenza surveillance networks to countries where none exists, the enhancement of the quality of surveillance in other countries to enhance outbreak detection, seroprevalence studies in populations at risk for avian influenza such as poultry workers, and enhanced outbreak response.

Scientific Research

Federal agencies have been very active in scientific research on avian influenza. Scientists at HHS and USDA have collaborated to successfully reconstruct the influenza virus strain responsible for the 1918 influenza pandemic. The findings from this research will greatly advance preparedness efforts for the next pandemic. Previously, influenza experts had limited knowledge of factors that made the 1918 pandemic so much more deadly than the 1957 and 1968 pandemics. One of the most striking features of the 1918 pandemic was its unusually high death rate among otherwise healthy people aged 15 to 34. In reconstructing the virus, the researchers are learning which genes were responsible for making the virus so harmful. This is an important advance to strengthen preparedness efforts, because knowing which genes are responsible for causing severe illness can help scientists develop new drugs and vaccines that focus on the appropriate targets.

Additionally CDC researchers have conducted studies on the incidence of adamantane resistance among influenza A viruses isolated worldwide from 1994 to 2005. Adamantanes are antiviral drugs that have been used to treat influenza A virus infections for many years. However, their use is rising worldwide, and viral resistance to the drugs has been reported among influenza A viruses (H5N1) strains isolated from poultry and humans in Asia. This data raises questions about the appropriate use of antiviral drugs, especially adamantines, and draws attention to the importance of tracing emergence and spread of drug resistant influenza A viruses**.** It is important to note that, although the H5N1 viruses isolated from people in Asia during the past two years appear to be resistant to adamantanes, they remain sensitive to neuraminidase inhibitors such as oseltamivir (Tamiflu®).

Development and Manufacture of Vaccine

Another important research area is vaccines: seeking improved strategies to enhance their development, manufacture, distribution and delivery. The development and role of a pandemic influenza vaccine is a principal component of the HHS Pandemic Plan, which I will describe later in the testimony. During an influenza pandemic, the existence of influenza vaccine manufacturing facilities functioning at full capacity in the United States will be critically important. We assume the pandemic influenza vaccines produced in other countries are unlikely to be available to the U.S. market, because those governments have the power to prohibit export of the vaccines produced in their countries until their domestic needs are met. The U.S. vaccine supply is particularly fragile; only one of four influenza vaccine manufacturers that sell in the U.S. market makes its vaccine entirely in the United States; one other makes some of its vaccine in the United States.

Another important factor is that public demand for influenza vaccine in the United States varies annually. Having a steadily increasing demand would provide companies with a reliable, growing market that would be an incentive to increase their vaccine production capacity. In FY 2006, CDC will direct $40 million through the Vaccines for Children (VFC)

program to purchase influenza vaccine for the national pediatric stockpile as additional protection against annual outbreaks of influenza. These funds to purchase vaccine can be used if needed during annual influenza seasons or possibly in a pandemic situation. HHS has also signed a $100 million contract with sanofi pasteur to develop cell culture vaccines. In addition, the President is requesting $120 million in FY 2006, an increase of $21 million, to encourage greater production capacity that will enhance the U.S.-based vaccine manufacturing surge capacity to help prepare for a pandemic and further guard against annual shortages.

Funds from the Strategic National Stockpile (SNS) have purchased approximately two million bulk doses of unfinished, unfilled H5N1 vaccine. This vaccine has not yet been formulated into vials, nor is the vaccine licensed by the HHS Food and Drug Administration. Clinical testing to determine dosage and schedule for this vaccine began in April 2005 with funding from NIH. Initial testing shows that, in its current form, a much higher dose of vaccine, up to 12 times as much as originally predicted, will be needed to produce the desired immune response in people. HHS therefore is supporting the development and testing of potential dose-sparing strategies that could allow a given quantity of vaccine stock to be used in more people. These strategies include developing adjuvants—substances added to a vaccine to aid its action—and the possibility of using intradermal rather than intramuscular injections. Such studies are currently underway, funded through the NIH. Additionally, HHS recently announced the award of a contract to the Chiron Corporation for the development of an H5N1 vaccine.

One of the main efforts by HHS in pandemic preparedness is to expand the nation's use of influenza vaccine during inter-pandemic influenza seasons. This increase will help assure that the United States is better prepared for a pandemic. Influenza vaccine demand drives influenza vaccine supply. As we increase annual production efforts, this should strengthen our capacity for vaccine production during a pandemic. We are also developing strategies to increase influenza vaccine demand and access by persons who are currently recommended to receive vaccine each year.

Domestic Preparedness

HHS Pandemic Influenza Plan

On November 2, 2005, the *HHS Pandemic Influenza Plan* was released. The HHS Plan is a blueprint for pandemic influenza preparedness and response and provides guidance to national, State, and local policy makers and health departments with the goal of achieving a national state of readiness and quick response. The HHS plan also includes a description of the relationship of this document to other federal plans and an outline of key roles and responsibilities during a pandemic. In the event of a pandemic and the activation of the National Response Plan, the CDC has a critical role to support the Department of Homeland Security in their role of overall domestic incident management and Federal coordination The President is requesting additional FY 2006 appropriations for HHS totaling $6.7 billion in support of the *HHS Pandemic Influenza Plan*. In seeking this funding, the goals are: to be able to produce a course of pandemic influenza vaccine for

every American within six months of an outbreak; to provide enough antiviral drugs and other medical supplies to treat over 25 percent of the U.S. population; and to ensure a domestic and international public health capacity to respond to a pandemic influenza outbreak.

In addition to outlining the federal response in terms of vaccines, surveillance, and planning, the HHS Pandemic Influenza plan makes clear the role of individual Americans in the event of an influenza pandemic. The importance of such ordinary but simple steps as frequent hand washing, containing coughs and sneezes, keeping sick children (and adults) home until they are fully recovered are widely seen as practical and useful for helping control the spread of infection. The plan also describes options for social-distancing actions, such as "snow days" and alterations in school schedules and planned large public gatherings. While such measures are, ordinarily, unlikely to fully contain an emerging outbreak, they may help slow the spread within communities.

State and Local Preparedness and Planning

All states have submitted interim pandemic influenza plans to CDC as part of their 2005 Public Health Emergency Preparedness Cooperative Agreements. Key elements of these plans include the use of surveillance, infection control, antiviral medications, community containment measures, vaccination procedures, and risk communications. To support the federal and state planning efforts, CDC has developed detailed guidance and materials for states and localities, which is included in the HHS Plan. CDC will work with states to build this guidance into their plans. CDC has taken a lead role in working with the Advisory Committee on Immunization Practices (ACIP) and the National Vaccine Advisory Committee (NVAC) which recommend strategic use of antiviral medications and vaccines during a pandemic when supplies are limited.

CDC is working to: (1) ensure that states have sufficient epidemiologic and laboratory capacity both to identify novel viruses throughout the year and to sustain surveillance during a pandemic; (2) improve reporting systems so that information needed to make public health decisions is available quickly; (3) enhance systems for identifying and reporting severe cases of influenza; (4) develop population-based surveillance among adults hospitalized with influenza; and, (5) enhance monitoring of resistance to current antiviral drugs to guide policy for use of scarce antiviral drugs.

Collaboration with the Council for State and Territorial Epidemiologists (CSTE) has considerably improved domestic surveillance through making pediatric deaths associated with laboratory-confirmed influenza nationally notifiable, and by implementing hospital-based surveillance for influenza in children at selected sites. CDC will continue to work with CSTE to make *all* laboratory confirmed influenza hospitalizations notifiable. Since 2003, interim guidelines have been issued to states and hospitals for enhanced surveillance to identify potential H5N1 infections among travelers from affected countries, and these enhancements continue. Special laboratory training courses to teach state laboratory staff how to use molecular techniques to detect avian influenza have been held. In the past year, CDC trained professionals from all 48 states that desired training.

Healthcare System

If an influenza pandemic were to occur in the United States, it would place a huge burden on the U.S. healthcare system. Medical surge capacity may be limited, and could be vastly outpaced by demand. Healthcare facilities need to be prepared for the potential rapid pace and dynamic characteristics of a pandemic. All facilities should be equipped and ready to care for a limited number of patients infected with a pandemic influenza virus as part of normal operations as well as a large number of patients in the event of escalating transmission. Preparedness activities of healthcare facilities need to be synergistic with those of other pandemic influenza planning efforts. Effective planning and implementation will depend on close collaboration among state and local health departments, community partners, and neighboring and regional healthcare facilities. However, despite planning, in a severe pandemic it is possible that shortages in staffing, beds, equipment (e.g., mechanical ventilators), and supplies will occur and medical care standards may need to be adjusted to most effectively provide care and save as many lives as possible.

CDC has developed, with input from state and local health departments and healthcare partners, guidance that provides healthcare facilities with recommendations for developing plans to respond to an influenza pandemic and guidance on the use of appropriate infection control measures to prevent transmission during patient care. Development of and participation in tabletop exercises over the past two years have identified gaps and provided recommendations for healthcare facilities to improve their readiness to respond and their integration in the overall planning and response efforts of their local and state health departments. The healthcare system has made great strides in preparation for a possible pandemic, but additional planning still needs to occur.

Antiviral Drugs

A component of the HHS Pandemic Influenza plan is acquiring, distributing, and using antiviral drugs. CDC has been working to procure additional influenza countermeasures for the SNS. Because the H5N1 viruses isolated from people in Asia during the past two years appear resistant to one class of antiviral drugs but sensitive to oseltamivir (Tamiflu®), the SNS has purchased enough oseltamivir (Tamiflu®) capsules to treat approximately 5.5 million adults and has oseltamivir (Tamiflu®) suspension to treat nearly 110,000 children. The SNS also includes 84,000 treatment regimens of zanamivir (Relenza®). WHO recently announced that the manufacturer of Tamiflu®, Roche, has donated three million adult courses. These will be available to WHO by mid-2006.

Enhancement of Quarantine Stations

CDC has statutory responsibility to make and enforce regulations necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the United States. This effort includes maintaining quarantine stations. Quarantine stations respond to illness in arriving passengers, assure that the appropriate medical and/or procedural action is taken, and train Customs and Border Protection officers to watch for ill persons and imported items having public health significance. Currently, CDC's Quarantine Stations are actively involved in pandemic influenza preparedness at their respective ports of entry. CDC's goal is to have a quarantine station in any port that

admits over 1,000,000 passengers per year. We are expanding the nation's Quarantine Stations; staff now have been selected for 18 Stations and are on duty at 17 of these Stations. HHS and the Department of Homeland Security (DHS) have recently established a Memorandum of Understanding setting out specific cooperation mechanisms to combat the introduction and spread of communicable diseases. These include DHS assistance with passive and, in certain instances, active surveillance of passengers arriving from overseas, as well as information sharing to assist in contact tracing of passengers with communicable or quarantinable diseases. HHS/CDC will provide training and other necessary support to prevent disease from entering the United States.

Informing the Public

Risk communication planning is critical to pandemic influenza preparedness and response. CDC is committed to the scientifically validated tenets of outbreak risk communication. It is vital that comprehensive information is shared across diverse audiences, information is tailored according to need, and information is consistent, frank, transparent, and timely. In the event of an influenza pandemic, clinicians are likely to detect the first cases; therefore messaging in the pre-pandemic phase must include clinician education and discussions of risk factors linked to the likely sources of the outbreak. Given the likely surge in demand for healthcare, public communications must include instruction in assessing true emergencies, in providing essential home care for routine cases, and basic infection control advice. CDC provides the health-care and public health communities with timely notice of important trends or details necessary to support robust domestic surveillance. We also provide guidance for public messages through the news media, Internet sites, public forums, presentations, and responses to direct inquiries. This comprehensive risk-communication strategy can inform the nation about the medical, social, and economic implications of an influenza pandemic, including collaborations with the international community. We are working through the International Partnership on Avian and Pandemic Influenza and with the WHO Secretariat to harmonize our risk-communication messages as much as possible with our international partners, so that, in this world of a 24-hour news cycle, governments are not sending contradictory or confusing messages that will reverberate around the global to cause confusion.

Conclusion

Although much has been accomplished, from a public health standpoint more preparation is needed for a possible human influenza pandemic. As the President mentioned during the announcement of his *National Strategy for Pandemic Influenza*, our first line of defense is early detection. Because early detection means having more time to respond, it is critical for the United States to work with domestic and global partners to expand and strengthen the scope of early-warning surveillance activities used to detect the next pandemic. To monitor H5N1 viruses for changes indicating an elevated threat for people, we must continue to strengthen and build effective in-country surveillance. This must include continued enhancement of training for laboratorians, epidemiologists, veterinarians, and other professionals, as well as promotion of the comprehensive and

transparent reporting that is essential to monitor H5N1 and other strains of highly pathogenic avian influenza.

The outbreaks of avian influenza in Asia and Europe have highlighted several gaps in global disease surveillance that the United States must address in conjunction with partnering nations. These limitations include: 1) insufficient infrastructure in many countries for in-country surveillance networks; 2) the need for better training of laboratory, epidemiologic, and veterinary staff; and, 3) the resolution of longstanding obstacles to rapid and open sharing of surveillance information, specimens, and viruses among agriculture and human health authorities in affected countries and the international community. The International Partnership the President established is also looking at how best to solve these challenges.

During an influenza pandemic, the presence of influenza vaccine manufacturing facilities in the United States will be critically important. The pandemic influenza vaccines produced in other countries are unlikely to be available to the U.S. market, because those governments have the power to prohibit export of the vaccines until their domestic needs are met. The U.S. vaccine supply is particularly fragile. Only one of four influenza vaccine manufacturers selling vaccine in the U.S. market makes its vaccine entirely in this country. It is necessary to ensure an enhanced and stable domestic influenza vaccine market to assure both supply and demand.

Although the present avian influenza H5N1 strain in Southeast Asia does not yet have the capability of sustained person-to-person transmission, we are concerned that it could develop this capacity. CDC is closely monitoring the situation in collaboration with WHO, the affected countries, and other partners. We are using its extensive network with other federal agencies, provider groups, non-profit organizations, vaccine and antiviral manufacturers and distributors, and state and local health departments to enhance pandemic influenza planning. Additionally, the national response to the annual domestic influenza seasons provides a core foundation for how the nation will face and address pandemic influenza.

Thank you for the opportunity to share this information with you. I am happy to answer any questions.